THE MÜTTER LECTURES ON SELECTED TOPICS IN SURGICAL PATHOLOGY.

SERIES OF 1890-1.[1]

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LECTURE II.

WOUND INFECTION AND SUPPURATION.

SYLLABUS.—*Predisposition to Infection, continued.*—Influence of manner of inoculation and arrangement of tissue; of irritating chemical substances. Miscellaneous influences. Variation in susceptibility. Concurrent growth of various bacterial species. Recognition of pyogenic cocci in the blood as an aid to diagnosis.

A Study of Pus.—What is pus? Different substances to which the name has been applied. Study of its gross and minute appearances, and circumstances under which it is produced. Virchow's views as to physiological and pathological irritations, and his four degrees of the inflammatory process. Old "humoral" theory. Cohnheim's teachings and their influence. Can we have pus without micro-organisms? Experiments with cadaverin. Study of the discharge from granulating wounds. Differences between acute and chronic abscesses, and the material they contain. Metastatic abscesses and *loci minoris resistentiae*. Minute anatomy of abscess.

The "pyogenic membrane" should be called "*pyophylactic*" membrane. Differentiation of so-called pus into true *pus*, *puruloid* and *archepyon*. Conclusions.

POINT OF INOCULATION AND ARRANGEMENT OF TISSUE.

BACILLI vary very much in their pathogenic effects, depending largely on the point where introduced, and the character of the tissue in which they are placed. Some

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organisms will not grow at large in the body, but only in certain tissues, while the character of the lesion may vary within wide limits, according to that of the tissue in which they thrive. The higher fungi act to best advantage within capillary blood vessels or large serous sacs. The bacillus of malignant œdema grows only in the cellular tissue, and the cocci of erysipelas thrive best in the lymphatic vessels and cellular tissue. Cheyne had some very suggestive results in experimenting with the *proteus vulgaris*, which is a common saprophytic organism. Introduced in quantity into subcutaneous tissue it provoked only abscesses, but the same amount introduced into the muscles would prove fatal, while a very small dose in the muscles was sufficient to produce abscess. He suggests that possibly some chemical substance in the muscle is split up and gives rise to poisonous compounds. Analogous results have been obtained with other bacteria. Fehleisen states that about one-twelfth of the quantity of staphylococci which is necessary to provoke peritonitis will cause suppuration in and around joints. He thinks also that pus varies in virulence according to its origin, different tissues probably producing different ptomaines. As affording the best illustration of the above statement Cheyne adduces the disease known as the *Black-leg* in England, *Rauschbrand* in Germany, or *Symptomatic anthrax* in France. It affects chiefly cattle and sheep, and is characterized by the rapid appearance of irregular nodules in the skin and muscular tissues, these being at first tense and very painful, but rapidly becoming painless and crepitating. It is accompanied by fever, usually high, but is generally fatal in from 36 to 40 hours. It is caused by anærobic bacilli, which are remarkable for the conditions by which they produce death. In order to affect the animal to this extent, they must be introduced either into the subcutaneous tissue or into the muscles. If injected into the veins or the bronchi they do not kill, but apparently die out after a little, leaving the animal protected against the disease. If after the virus has been injected into the veins a bruise is caused in some part of the body, the bacilli reach that spot and set up the disease. Inoculations made at the tip of the tail in cattle cause only a small amount of reaction. The nearer

the body the more marked the disturbance. All of which is to be explained partly by the dense tissues of the tail, and partly by the low temperature of the part, since if after inoculation the tail be wrapped in bad conductors of heat the reaction can be very much increased, and *vice versa.*

So far as the pyogenic organisms are concerned, most of them act in the cellular tissue, to which they gain access commonly after removal of the epithelium. The gonococcus appears to be the only bacterium which can penetrate uninjured epithelium, and even this only attacks certain mucous membranes. Bumm has shown that pure gonorrhœal pus may be injected into the subcutaneous cellular tissue without causing reaction, which proves that pus, apart from the microorganism contained in it, is not itself pyogenic. Moreover in such a case, if an incision into the part be made twenty-four hours later, the pus cells will be found in good condition, while the cocci have disappeared, which would seem to indicate a phagocytosis in this instance at least. As seen elsewhere, the pus of gonorrhœal buboes contains, not the gonococcus, but the ordinary pyogenic organisms, showing that such buboes are the result of mixed infection, the same being true of periurethral abscesses.

We have also evidence that the arrangement of tissue influences pyogenic action in the frequency with which pyæmia follows acute osteomyelitis. This is apparently due in large part to the great pressure to which pus is subjected in the interior of bone, and this high pressure is proven by the manner in which fat oozes out of bone when it is trephined; also by the occurrence of fat embolism in the lungs. There are numerous other illustrations, if one needed to introduce them, which go to show that bacteria appear to exercise certain selective affinities which are to be explained, we must suppose, by certain peculiarities in the tissues selected. The same is true of the higher fungi, like the pathogenic forms of mucor and aspergillus, the latter in the rabbit selecting the membranous labyrinth; which selection, in this instance, affords us an explanation of the rotary motion so characteristic of this disease in rabbits.

Irritating Chemical Substances.—These, when concentrated,

destroy the vitality of tissues, and when more dilute, set up at least the early stage of inflammation. The effect of such substances in producing a weak spot is no doubt the explanation of Kocher's result concerning acute osteomyelitis. He induced digestive disturbances by introducing large quantities of septic material into the intestinal canal. He then injured a bone by injecting ammonia or some other chemical substance into it, after which acute osteomyelitis occurred at the seat of injury, while the one disturbance without the other produced only temporary reaction. Experiments in the same direction, but slightly varied, give always the same result. The bearing of these investigations upon the development of blood poisoning in human beings can hardly be overestimated, and we shall have more to say about it when speaking of intestinal toxæmia. Cheyne argues from such facts as these that it is questionable whether, in granulating wounds which have become septic, it is well to wash them out with irritating antiseptics, as we so often do, unless these solutions are able to kill all the microorganisms present in the wounds, and thus render them aseptic, fearing lest the chemicals might so far injure the granulation wall as to produce a weak spot in which pyogenic cocci might develop, and from which they might enter the circulation. Thus it has been found that in cases of tubercular abscesses of bones and joints disseminated tuberculosis occurs much more frequently where the sinuses have become septic, and more especially where these septic sinuses have been much irritated by inutile antiseptic injections. So he would avoid the use of carbolic acid, for instance, and simply wash away the discharge with some fluid which will not injure the granulation wall. Considering the known properties of peroxide of hydrogen, this may be an indication for its use in these cases. Of course, except in the case of wounds, the chemical substances, by aid of which bacteria gain a foothold, are themselves products of bacterial action. That many of these are wholly poisonous is now well known. Two of the ptomaines which have been most commonly experimented with are cadaverine and putrescine. These are products of putrefactive bacteria, rather than of the pyogenic. As we shall show later the pyoid material which has occasionally been

found after the introduction of cadaverine is not entitled to the name of pus, when it is, as it has been stated to be, sterile, since, according to the view adopted in these lectures, there is no fresh pus which is free from organisms. So far as the pyogenic cocci are concerned, Brieger states that he has been unable, at least until recently, to obtain from cultivations of these organisms, any true toxine. When the staphylococcus aureus or albus is cultivated on moist beef or veal, ammonia is given off, and the latter produces in addition tri-methylamine, the streptococci likewise producing both of these substances.

Ammonia is naturally irritating. The latter is closely allied to the ptomaines, and when present in considerable quantity is noxious. When these bacteria are cultivated in milk they rapidly set up pure lactic fermentation. This fermentation undoubtedly takes place in wounds, causing acidity of discharge and watery or very thin pus. That fever in suppurative disease may be explained by increased tisssue change as the result of bacterial growth without the necessary production of ptomaines, may be argued by analogy, as Baumgarten states in the case of the fever which occurs in trichinosis, where there is no idea of the action of ptomaines.

(Leber, a couple of years ago, claimed to have recovered from cultivations of staphylococci a crystalline substance which he called phlogosine, and which he said produced pus when injected into animals. *Fortschritt d. Med.*, 1888, No. 12, But since his publication we have heard little or nothing of this substance.)

Certain other influences also exert a decided effect in favoring suppuration, many of which figure prominently in the condition of the blood. Furuncle, carbuncle and other suppurative affections are known to occur frequently in cases of diabetes. Very recently Bujwid (*Centblt. f. Bakter.*, Vol. 4, p. 577) has studied this matter experimentally. He first found that staphylococci do not grow well in media containing 5% of grape sugar. He then ascertained that a given number of these cocci, insufficient to cause an abscess when injected alone, will do so when injected along with the fluid containing 25% of grape sugar. Also that a given quantity along with

12% of grape sugar did no harm; but that if in another animal the same quantity was injected and then a 12% solution of grape sugar was injected daily at the same spot, an abscess formed. Variations of these experiments, and their confirmation by Karlinski, show that the presence of grape sugar in the tissues so depresses their vitality that the pyogenic cocci can act in much smaller numbers and more vigorously than would otherwise be the case.

Dilution of the blood also interferes to some extent with the rapidity with which bacteria are killed in it. If water in quantity be injected along with non-pathogenic bacteria, they do not disappear from the blood so quickly as when injected without it. For other causes which may be included under this caption we must refer to Cheyne's excellent monograph.

There are extraordinary variations between different animals in regard to susceptibility, which are extremely significant. For instance, in the case of mouse septicæmia, a mouse will die as a result of the injection of a single bacillus, while a rabbit will tolerate the injection of 4cc. of jelly cultivation, containing millions of bacilli, with only slight local symptoms of swelling and redness. So too with so-called chicken cholera. A single organism is enough to determine the death of a rabbit but two or three hundred thousand are necessary to kill a Guinea pig; while ten thousand may produce an abscess, and less than that number have no perceptible effect. Cheyne has deduced from such results as these certain laws which he formulates as follows:

1. The pathogenic dose of a virus varies inversely with the predisposition of the animal to the disease in question.

2. In animals which are not very susceptible to a disease, the severity of the infection varies directly, within certain limits, with the amount of virus introduced.

Some as yet unexplained phenomena must be grouped under the heading of increased virulence,—a phenomenon well-known to all but quite inexplicable. For instance with regard to the bacilli of symptomatic anthrax, it has been found that the addition of a minute quantity of lactic acid to cultures increases the virulence of very attenuated virus in a short time, even one-fifth of one per cent will double their virulence in

twenty-four hours. So the pyogenic cocci when grown in milk produce lactic acid, although there is no evidence that their virulence is thereby increased. Ogston discovered that if he grew pyogenic cocci in eggs, their activities were notably augmented. On the other hand, lactic acid does not increase the activity of the pneumococcus which loses its virulence most quickly when grown in milk. Such facts may not yet have a practical bearing for us, yet they show by what slight and unexpected causes virulence may be altered. Experimenters are well aware of the changes produced by passing organisms through animals. For instance, Pasteur discovered that the bacilli of swine erysipelas are weakened by passing through pigeons, while the bacilli of rauschbrand are strengthened by passing through very young guinea pigs from one to three days old. The results of passing anthrax through animals, as well as of the unknown contagium vivum of hydrophobia, are well known. Also that in order to keep cultures of bacillus tuberculosis active they must be passed through animals every three or four generations.

Anthrax bacilli, in minutest doses, in mice, guinea pigs, etc., produce a rapid general, septic, fatal infection; in dogs and in older or larger animals very small doses have little or no effect, and larger ones cause carbuncle or œdema. In man they cause usually only malignant pustule, which has seldom any marked septic effect. The pnemonococcus when injected into the tissues of mice and rabbits produces a rapidly fatal septicæmia; only when injected into their lungs does it cause pneumonia.

So with the pyogenic cocci. Often after their injection in dogs no result follows. In man the item of individual susceptibility is one of great importance and at the same time of great variability. The immunity from septic complications which the wounded Turks displayed during the Turko-Russian war was remarked upon by German military surgeons. Undoubtedly they were not lacking in opportunities for developing sepsis, yet they displayed such vital habits as made their bodies unfavorable soil for bacterial development.

Or to put this same idea in the words of Prof. Welch (in a private communication): "The pyogenic cocci are a curious

group of organisms which it is difficult to bring into line, as regards their pathogenic properties, with other infectious bacteria. Their effects seem to vary strikingly with their degree of virulence, with the number inoculated, with the place and manner of inoculation, and with those mysterious conditions which we call predisposition but which we little understand. And then, what a variety of pathological conditions they are capable of producing—from an innocent pustule to the most malignant pyæmia or ulcerative endocarditis."

It is of no small importance to consider the effect of the simultaneous growth of two or more species, by which pathogenic power may be at one time increased, at another diminished. In man, in all probability, pyogenic activity is thereby increased as is shown by the frequency of mixed infections. For instance, in wounds to which numerous species have had access a struggle probably results that terminates in favor of the pyogenic cocci, and this may be further complicated by the activity of saprophytic forms. Thus the foul smell of a wound, if present at all, usually subsides as time goes on, especially if drainage be good, showing that putrefactive bacteria gradually cease their activity. Nevertheless the ptomaines produced by the latter, when taken into the system, depress the vitality of the patient, and thus better fit these tissues to support the pyogenic cocci; while locally such products are injurious, as elsewhere described, owing to granulation tissues about the wound, and thus may open the way for systematic pyogenic infection. So Cheyne states that if a sinus leading to carious bone, whose wall is lined with membrane containing tubercle ('pyophylactic'), becomes infected by these cocci the result is a more rapid growth of the tubercle bacilli, by whose development general infection is made more probable, *i. e.*, local depression of vitality enables the tubercle bacilli to grow more luxuriantly. We shall have more to say on this subject when dealing with the subject of mixed infection.

The concurrent growth of bacteria is perhaps in no place better illustrated than in the pus coming from a wound which has produced tetanus. When speaking of this disease we shall call attention to the method by which the bacilli of tetanus may be isolated from other forms; but so far as their co-

existence is concerned we have a significant demonstration of the simultaneous growth of aerobic and non-aerobic organisms; the former consuming the limited amount of oxygen present, and really producing the conditions necessary for the best growth of the bacillus of this dread disease.

Perhaps one finds no more conspicuous illustration of the various degrees of immunity enjoyed by different animals than can be met with in the susceptibility of different species to anthrax. A single bacillus introduced into a guinea pig certainly proves fatal, while rats often survive inoculation, apparently suffering little or not at all, this depending largely upon the age of the animal. The older the rat the fewer general symptoms does it manifest; the thicker the pus met with at the seat of the injection, the more rapidly do the anthrax bacilli perish.

There are other times when it is to the advantage of the patient to be the host of more than one species of pathogenic organism, thus taking advantage of certain antagonisms—some of which are well known. Emmerich has shown the value of the cocci of erysipelas, in rabbits, as protective against anthrax and even curative. His experiments have been confirmed by Mattei and by Pawlowsky, and the latter found no small degree of antagonism between anthrax bacilli on the one side and the micrococcus prodigiosus and the pneumococcus on the other. Whether the explanation be that the cocci by themselves prevent the growth of the bacilli, or that they irritate the phagocytes and increase their destructive power, or whether there is produced some chemical substance which is poisonous to the bacilli, is not known. It suggests, at all events, a possible treatment for anthrax in man by inoculation with erysipelas, and it at least raises the question whether, if tumors are really of parasitic origin, the well-known fact that they sometimes disappear after a local erysipelas, or after an erysipelas deliberately produced by inoculation, may not enjoy the same explanation. It will be seen further that the treatment for phthisis, by inhalation of non-pathogenic organisms, as already tried, may, after all, have a rational basis, although so far unsuccessful.

Duclaux, in his work on "Microbes and Disease" gives an

excellent example of the part played by other factors in relation to infection. The itch of domestic animals is produced by an acarus which may be almost seen with the naked eye, and which lives in the superficial layers of the skin. According to the experiments of Delafond and Bourgingnon, this insect when placed on the skin of well nourished healthy animals does not penetrate nor propagate. Healthy sheep cannot be artificially inoculated with itch, but if they are first submitted to unhealthy surroundings as regards nourishment and stabling, then the acarus can be very readily implanted, and will flourish so long as the animals are thus kept. Just so soon as their nutrition is improved and their stalls cleaned and aired, then without treatment against the acarus the itch disappears, and the animal becomes clean. The same differences notably affect the silk-worm in France. The disease known as *pebrine* attacks silk-worms, irrespective of their state of health, while *flachérie* attacks worms only whose digestive apparatus is weakened by disease or heredity.

The recognition of pathogenic cocci in the blood, as an aid to diagnosis.—The statement has been already made, and is confirmed by so many observers, that the normal blood of healthy animals does not tolerate the presence of pathogenic organisms nor harbor them, that it scarcely needs repetition here. Nevertheless, it is well-known that two propositions, each the converse of the other, may be accepted as true; first, that, in a condition of lowered vitality, they may be present in the blood, and second, that when met with in the blood, they are significant portents of impending evil. Although this has been in a general way recognized for some time, Eiselsberg has been perhaps the first to make practical application of the fact and to introduce to the profession a new diagnostic aid of some practical utility.

In the *Wiener klin. Woch.*, September 18, 1890, he has reported four cases of supervention of high fever after injury or operation, where the diagnosis of impending or present septicæmia was made by a bacteriological examination of the blood, and confirmed by subsequent events. That such an aid to diagnosis is not usually called for, will be generally allowed, yet that it may have no small value is illustrated by

one of his cases, where for some days diagnosis wavered as between an actual rheumatic affection, and osteomyelitis—in which the discovery of pathogenic cocci in the blood and their successful cultivation both cleared up the case, and furnished an important indication for operation. In three of these cases staphylococci were found, in the other streptococci. Aside from these instances in which the examination had a diagnostic value, he reports several other undoubtedly septic cases;—for instance, three progressive phlegmons, one acute osteomyelitis and four cases of septic peritonitis, which were carefully examined, and in three of them staphylococci were found. He alludes also to the rapidity with which these organisms develop in the blood after death, and reports a most interesting series of *post-mortem* observations in which cultures were made from the blood of an individual dying of sepsis, at intervals of 10 minutes, during the two hours immediately succeeding death, from which it appeared that they developed at an almost arithmetical ratio.

Having now discussed at some length the causes which predispose to infection we are better prepared for an attack upon the obscure, and yet tremendously important topic, of suppuration or the formation of pus and a rehearsal of some of its properties and varieties.

Suppuration and Pus.

What is pus? A few years ago this question was comparatively easily answered. That it is now a query to which it is extremely difficult to give an explicit answer, is simply an evidence of progress in the study of pathology. A former and revered teacher used to express it tersely that "pus is dead or dying blastema." Even the term blastema is now almost obsolete. According to Robin, blastema means "the substance resulting from the elaboration of nutritive material furnished to the anatomical elements by the blood." Foster's dictionary gives as other definitions: "Undifferentiated embryonic tissue; the material out of which a part is to be formed;" and, "a free or parenchymatous plastic exudate." These definitions are sufficiently succinct to indicate that dead or

dying blastema must be good and valuable material going or gone to the bad. In a rough and off-hand way, therefore, this conception of the term pus may be considered sufficient as a working basis for a further study of the substance itself.

But, as generally used by the clinician, the term is applied alike to the contents of acute or cold abscesses, which have never known exposure to the air, to the discharge from mucous, as well as granulating surfaces, and to the fluid or semi-solid results of degeneration of various tissues. Are these various substances identical, and do they deserve the same name? This is a vexed subject in the domain of surgical pathology, to a discussion of which the balance of this lecture is in the main devoted.

Many and many a time have I seen my operation wounds heal by primary union, under an aseptic dressing. Of them I could say, as we usually do under such circumstances, they healed without suppuration. And yet, if the drainage tube—supposing one had been used—had been left *in situ* a few hours too long, there would be found about its opening, or in its lumen, a drop, perhaps a few drops, of creamy, semi-solid material, which we should ordinarily call pus. Is this material identical with the pus from an acute abscess? To this inquiry I have devoted no small time and study, both at the desk and in the laboratory, and such conclusions as I have reached shall appear further on.

There is a popular expression: "There are dogs and dogs." Must we not say also, "There is pus and pus."

This subject can only be approached by a careful study of the gross and minute appearances of pus, and the circumstances under which it is produced. A study by which these questions may be answered is inseparable from a study of inflammatory phenomena, with which I must then, for a little while again detain you.

Virchow has made this distinction between physiological and pathological irritation (Reiz), that in the former case the function of the cell, or the collection of cells (the organ), is simply increased; in the latter it is disturbed. The entire process by which an alteration or disturbance of nutrition is thus brought about by irritation he considers to be a progress-

ive process, but not necessarily an inflammation. It might result in hyperplasia (numerical cell-increase), inflammation, or tumor formation. He classified irritations as mechanical, chemical and physical, *i. e.*, thermic and electrical. Only such irritations as lead to inflammation interest us here, and, as we shall see, in considering pus formation that we shall have to practically limit ourselves to a consideration of micro-organisms as the sole causes of such irritation.

At that time (1870) Virchow distinguished four degrees of the inflammatory process:

1. A form distinguished—aside from changes in the cells themselves—by watery, serous, albuminous, or muçinous exudate.
2. A form in which the exudate is fibrinous (croupous).
3. A form in which pus is produced.
4. A form characterized by hæmorrhagic exudate.

He considers these as progressive stages of one and the same kind of irritation, belonging to either of the three classes before named.

Applied to the study of repair of wounds, this doctrine taught that mechanical irritation (which caused them) alone was sufficient to explain the formation of pus, that it was unnecessary to seek further for its cause, and that tumefaction of the wound edges bears the same relation to failure to secure primary union that suppuration does to healing by granulation. This opinion seemed the more plausible since the wounds whose borders presented least tumefaction were those which healed most kindly *per primam.*

Attack upon this doctrine was speedy and determined. Cohnheim had published in 1867 his studies of the diapedesis of the leucocytes, and the importance of this publication, as well as its accuracy, were almost universally recognized; while the leading part heretofore played by the connective tissue corpuscle, according to Virchow's views, had now, at least, to be shared by the wandering leucocyte. This opinion has been since strengthened, to the point of conviction, by the labors of Cohnheim, Ziegler, and their scholars, so that now it is possible to find an explanation of such neoplasms as belong to the

category of inflammatory, regenerative, hyperplastic or callus, in the known properties of the leucocyte.

I say it is now possible, even probable, but hold that as yet we are not in position to go to extremes. Cohnheim's enthusiastic followers claim that Virchow has considered innumerable cells to be descendants of connective tissue corpuscles, which are in fact escaped leucocytes. Even granting this, there has been no sufficient evidence yet adduced to show that the connective tissue cells are necessarily or absolutely passive, and take no part in cell proliferation. Consequently, it seems as if, in this controversy, the middle ground is certainly the safer.

But the attacks upon Virchow's dicta were made not alone by the histologists, but by those who, like Klebs, contested them upon etiological ground. By 1872, in Germany, the Listerian system had been pretty well adopted, and there no longer remained a doubt but that wound suppuration was caused by contamination of instruments, fingers, dressings, etc., with bacteria. Other infectious inflammations, *e. g.*, endocarditis, erysipelas, were correctly ascribed to microbes, and, in 1878, appeared Koch's masterly work on "Wound Infection." Now, the importance of mechanical, chemical and physical irritations, as agents producing suppuration, was lost in the overwhelming magnitude of the freshly studied "specific reaction (suppuration) due to a specific virus." To be sure, Virchow retorted, in 1880, that we did not know the exact nature of this specific reaction, and that it must be either chemical or mechanical, which is undeniable, yet it is equally undeniable that bacteria did not figure as irritants, when he so fully discussed the causes and consequences of inflammation, and that he remains to-day rather a skeptic as to some of the new teachings in this respect.

The introduction of the antiseptic method has effected both a revolution and a revelation. It was till lately held that the bacteria of putrefaction were also at the same time the pyogenic. In 1881 Virchow and his scholars claimed that suppuration was not invariably produced by micro-organisms and by them alone, but that when it displayed a milder form, less progressive, it was brought about by purely mechanical

causes, fractures, wounds, etc. But the researches of Ogston, Rosenbach, Passet, and numerous other close and diligent observers, clearly demonstrated that suppuration has but one cause, that it is of parasitic origin, and that the pyogenic bacteria are not to be confounded with the saprogenic or putrefactive.

Studies directed especially to the elucidation of these hotly-disputed questions resulted in unexpected advance. Strassburger, Fleming and others found that the nucleation which precedes cell proliferation afforded an interesting subject by itself, and karyokinesis is now a well recognized link in the chain of cell progression. Not alone in the leucocytes is the karyokinetic process known; it has been studied in the connective tissue cells by Scheltema, Grawitz and Ribbert. This fact lends additional argument in favor of a position midway between the extremes of Virchow and Cohnheim. Whether the inflammatory irritant acts primarily upon the connective tissue elements, the capillary vessels, the muscular and the fatty tissues, whereby active hyperæmia and diapedesis of leucocytes are excited, or whether the reverse is true, will depend upon whether one sides with Virchow in the former case, or with Cohnheim and Weigert in the latter.

According to the views of the humoral pathologists, of whom Rokitansky was the father, pus corpuscles, which were seen in the exudate known to have left the vessels, were supposed to have originated from it, hence the definition of their day—"pus is dead blood." The ultimate cause of inflammation and suppuration was sought in the chemical condition of the blood; and the dyscrasiæ, or varieties of badness of the blood, were hence considered the causes of these phenomena. Although the old humoral pathology is now abandoned, it will be seen that it, nevertheless, took cognizance of certain truths, since such dyscrasiæ as diabetes, syphilis, and gout are well known to be predisposing causes of inflammation.

It was Virchow who decently interred this humoral doctrine, by showing that the formation of cells out of such exudates alone was impossible. By establishing the dictum *omnis cellula e cellulo*, he founded the new cellular pathology, which was to medical science what Keppler's laws were to astronomy.

Proliferation of cells now accounts for all tissue changes, though, by itself, it fails to supply all the knowledge of causes for which we earnestly yearn.

The misinterpretion of certain cellular phenomena by the cellular pathologists has been, in great measure, atoned for by the discoveries of Cohnheim and his pupils, who repeated, in every possible way, the observations first made in 1848, by Waller and Wallace, and who not only established the fact of the diapedesis in the leucocytes, but showed the vast importance of this process in explaining inflammatory action. If they, in their enthusiasm, claimed for their observations a solution of the whole question, they simply showed themselves human, and so liable to err.

While we are not, even to-day, in position to do more than calmly survey the fields where the pathologists of the recent past have excitedly contended for the accuracy of their own notions, yet we must admit that somewhat of truth was contained in the humoral doctrine, and that Virchow and Cohnheim are both right and both wrong; wrong, however, mainly in each trying to explain everything upon his own discoveries and in refusing to see as much of the truth in the teachings of his opponent as in his own.

The question may perhaps be legitimately raised whether it is possible to have acute abscess formation without the action of micro-organisms. The answer to this question should cover two different phases of the subject. First, it remains to be proven that sterile pus, providing it be ever met with, is really entitled to be considered pus, since it can in no wise be infectious, and since ordinary pus owes its principle characteristics to the bacteria which it contains. In the second place it does not necessarily follow, because no bacteria are found in pus at the time of its evacuation, that they were not present in the beginning as active agents. Thus Rosenbach examined the pus from two suppurating hydatid cysts, and found nothing, but that this is not usually the case is proved by the observations of several others. The pus from suppurating buboes following chancroid has occasionally been found free from organisms, and yet they are so nearly ever present in such cases as to imply an indisputable origin to such pus. Cheyne speaking

of these cases states that such abscesses are doubtless caused by the virus of a chancroid, a virus which is in all probability of bacterial origin, but not yet recognized. If, however, we believe with Sturgis and some others that chancroid is not due to a specific organism but rather to a practical manifestation of the activity of known pathogenic forms, the explanation afforded by Cheyne will fall to the ground. In this connection he states that DeLuca has described a very similar coccus, which he considers the virus of soft chancre, and which he named *micrococcus ulceris*. This organism is a typical ærobe, and he explains the fact, if fact it be, that these buboes are not infected until two or three days after they have been opened, by the theory that it is not until after the access of air has been permitted for two or three days that this organism attains its full activity. Could this be proven it would furnish a strong argument against early or free incision.

As will be seen throughout these lectures I am endeavoring to make an actual difference between pus such as comes from an acute abscess under ordinary circumstances, and which is due to and contains micro-organisms, and another material quite similar to it in macroscopic and even in microscopic appearance, which contains no bacteria, which has no infectious properties, which is not capable of causing sepsis, which is not met with clinically and almost never except as the result of laboratory experiments, which is a fibrinous exudate more or less rich in cells and due to the action of powerful chemical irritants, but which is not pus in the true sense of the term. Such material, which we will call, if you like, *pyoid* or *puruloid*, can be produced by the aseptic injection of sterile croton-oil, or turpentine, or cadaverin, or of certain other chemical poisons, and has been noted under these circumstances by so many experimenters that it is scarcely worth while to catalogue their names. It does not undergo the fate of true pus, and while it may remain for a time enclosed within the tissues, it undergoes no spontaneous evacuation as an abscess tends to extrude its contents. Where bacteria are at work they by their peptonizing action readily dissolve this material and prevent the coagulation of fresh exudates and the absorption of the old. On the other hand where bacteria are not at work

the tissues possess the power of dissolving and removing dead material, while such portion as cannot be removed is encapsulated and removed from further consideration.

(If any exception is to be made to the above statement it is with reference to cadaverin, which is stated by Grawitz and Scheuerlen to be not merely an irritant, but to prevent coagulation; but inasmuch as this is a ptomaine, we are, by its injection, reproducing, to a large extent, the conditions which would be furnished by bacteria if present.)

Grawitz has experimented carefully with *cadaverin*, which seems to combine the useful properties of an antiseptic and disinfectant with the undesirable powers of producing necrosis and inflammation. Two and a half per cent solutions destroy the pyogenic staphylococci after one hour's contact, and smaller proportions added to nutrient gelatine hinder or prevent their growth. Subcutaneous injections produce, according to their strength, necrosis, pseudo-suppuration or inflammatory œdema. In this pseudo-pus there are no pyogenic organisms. When five or ten per cent cadaverin solutions are mixed with pus cocci and then injected, the latter either die, or, as the injected fluid is reduced in strength by the tissue juices, they manifest their vicious propensities and cause acute phlegmons and abscesses. (*Virchow's Archiv.*, cx, p. 1).

Scheuerlen showed how solutions of cadaverin and putrescin, and various putrid substances, without aid from microorganisms, could evoke a pseudo-suppuration; which nevertheless had nothing progressive or infectious about it. (*Fortschrit. d. Med.*, 1887, No. 23, p. 762). Fehleisen, however, showed that all these ptomaines possessed the property of delaying or preventing coagulation of the blood, and then repeated Weigert's statement that the suppuration is in large measure an affair of limitation of this process.

There is yet another material analogous to pus which deserves brief consideration here. I allude to the puruloid exudate upon the surface of granulating wounds. This material is physiologically different from that which an acute abscess contains inasmuch as it represents a useful product, at least the remains of a useful product, since for the repair of all tissues which heal by granulation there is necessary a certain amount

of formative material, and this material can only come from pre-existing tissues, and must be supplied, at least in the main, from the blood. A quantity of leucocytes is constantly furnished to the granulating surface of which only a certain amount or proportion can be utilized. So many as are utilized undergo metaplastic changes, and become organized into tissue of a higher grade. Such of them as fail to be so utilized become the pyoid discharge from the healthy ulcer. Nowhere in connection with wounds is this fluid free from contact with the air, and consequently it is very likely to become infected on reaching the surface. If so infected it scarcely differs in any respect from true pus. If not so infected it will, nevertheless, show nearly the same constituents under the microscope, lacking only bacteria and necrotic shreds of tissue or debris. No granulating surface ever can cicatrize without the presence of a certain amount of this fluid. Unquestionably, however, irritating dressings or exposure to air, cause excess of discharge and infiltration of its cells.

In view of what has been said it will be seen that the true test as to the aseptic course of healing after a given operation or wound, is not so much as to whether any such puruloid material has been formed, but as to whether pathogenic bacteria have or have not been excluded. The typical aseptic primary healing of a fresh wound comprehends perhaps the absence of all puruloid discharge. Where, however, a drainage tube or drainage material has been introduced there will occasionally be found a few drops of gelatinous, creamy looking material upon the dressing, or obstructing the calibre of the tube, and this might easily give rise to the statement that such a wound had not healed, as enthusiasts claim it should under such dressings, without formation of a drop of pus. Some time ago, before I was aware of the investigations of others, I set myself the task of studying this matter in my own cases. It was at a time when I was using rubber drainage tubes much more than I do now in fresh aseptic cases. If upon the first dressing I met with any such material, cover glass preparations were made from it at once, and tubes of gelatine or agar were at the same time carefully inoculated with it. Subsequent observation of such cases has convinced

me that while this material is not necessarily always sterile, it is quite usual to find it so, and that many a wound goes through a typical aseptic course, from which, nevertheless, a small quantity of such fibrinous exudate may come, this exudate being due apparently to the irritation caused by a foreign body, mainly the drainage-tube or even the suture material.

Quite corroborative of my own studies are the investigations of Bossowski who undertook the examination of fifty wounds which had been protected by antiseptic (iodoform) dressings. Each fresh wound was irrigated during the operation and at its conclusion with a 3% carbolic solution, and the iodoform gauze to be applied next the wound was soaked in 5% carbolic solution. Of the wounds thus treated only one fifth (20%) remained free of organisms. About one-sixth (17%) showed themselves contaminated by non-pathogenic organisms, of which the *staphylococcus gilvus* was most important on account of its resemblance to the staphylococcus pyogenes aureus and albus. About one-half the wounds revealed the presence of the staphylococcus albus, although the majority of them healed *per primam*. The number of these cocci was very small. The balance of these contaminated wounds (about a third) showed trifling or limited suppuration. The other wounds not including the above showed that staphylococcus pyogenes aureus, or streptococcus pyogenes were present, and they all were suppurating.

He is inclined to consider that the so-called aseptic-wound fever of Volkmann and Genzmer is due to the circulation in the blood of some of these bacteria or their products. He reminds us that V. Eiselsberg found pyogenic bacteria in the blood of feverish injured or operated patients; (*vide* above).

Bossowski also investigated the material contained in the drainage-tubes removed five to seven days after operation. He cut off a piece with sterilized scissors and dropped it into the culture-tube. He found that the pale reddish, somewhat translucent, thick clot which the tube sometimes contains, as well as the clear, serous, reddish fluid which often escapes, were free from bacteria. The softened, dark red or dirty yellow secretions and detritus usually contained organisms. Of course

the plainly sero-purulent discharge always contained them. The researches of Staheli have also given about the same results.

After it was definitely understood that all surgical suppurations were of a parasitic origin, an effort was made to establish for the bacteria which caused them a property *sui generis*, as if they were neither chemical nor mechanical irritants, but possessed some hitherto unknown power. Such a theory prompted the investigations at once set on foot, during 1885-6, and conducted with most painstaking diligence by Hüter, Rosenbach, Orthmann, Lutton, and numerous others, to be referred to again, by which it was demonstrated that pure or sterile chemicals alone could never produce suppuration. Scheuerlen, Klemperer, Strauss, and others, have repeated these demonstrations, and have made conviction certain, that without bacteria or their products, suppuration never occurs. Some difficulty and confusion have arisen from the fact that it was found, in prosecuting these studies, that certain bacteria were pyogenic in the tissues of one animal, and not in those of another. Thus Grawitz and Dieckerhoff described a bacillus which thus varied in its effects according to the animal used.

In 1886, Grawitz and de Bary showed that very weak dilutions of pure cultures of the pyogenic bacteria (1 to 100, etc.), were resorbed without provoking suppuration. The daily use of ordinary solutions for hypodermic use is simply a homely illustration of this fact. They further showed that such active fluids as turpentine and strong nitrate of silver solution, which are of themselves actively parasiticide, when used upon certain animals in certain amounts, produced a fluid resembling pus. This fluid, however, contained no bacteria, lacked all the septic or infectious properties of true pus, and was produced under such conditions as never obtain, save in the laboratory of the experimenter, and at his pleasure only, at the expense of extreme precaution.

This is an appropriate place at which to stop, en passant, and ask whether it is fair to call such a fluid pus. Its like is not met with clinically, and the pus which we daily meet with, and which causes us so much trouble, is the pus which

we particularly study, and which is particularly deserving of the name.

Moreover, aside from Grawitz' and Scheurlen's results after the injection of Brieger's cadaverin, it is, furthermore, quite probable that other ptomaines besides cadaverin, all of which are of bacterial origin, may be found to have a similar effect, though several, at least, have failed so far to evince it. Let it be well emphasized just here, however, that even these few substances which thus have been shown capable of producing this puruloid material, do so only under the most favorable conditions of time, quantity, and species of animal used for experiment. Weak ammoniacal and cadaverin injections are resorbed; those of greater strength are followed by watery or albuminous infiltrations, or, sometimes, by exquisite fibrinous exudates; used still stronger, they cause hæmorrhage and this pseudo-suppuration; and, finally, when used in full strength, necrosis and gangrene are the consequences. It seems to me, upon both theoretical aud experimental grounds, that this puruloid fluid, to which I have above alluded, may be properly considered the product of the death of the cells, resulting from the inflammation set up as a result of the injection of the irritant, and the liquefaction of previously solid tissues, and that it is entitled to be considered pus only in the sense that it is dead blastema; whereas we all know that the pus with which surgeons meet and contend is something more than dead or even dying blastema; that it contains, at least when active and septic or infectious, living and lively organisms, whose activity and properties are most pernicious. Here is beautifully demonstrated the accuracy of one of Virchow's observations, which were, in the main, brilliant and comprehensive, that tissue reactions or changes are not characterized by wide distinctions; that pus-production is not to be considered, by itself, as a distinct process, but only as a stage in the various possible inflammatory changes in connective tissue. Adopting this view, we see that the differences between the formation of this puruloid fluid and of pus, consist, in a pathological sense, in the penetration into the tissues of destructive germs, and, in a clinical sense, in the overwhelming pathogenic importance which the tissues and the purulent material

now acquire by virtue of their presence and poisonous capabilities.

In clinical evidence of this feature, let me adduce the difference between an acute and a cold abscess. In the former the bacteria are still alive and actively producing poisonous material, in proof of which we have fever, sepsis, local destruction, even death. In the latter case, nature has thrown a sanitary cordon around the infected area in the shape of a thick investing membrane, the so-called but mis-named *pyogenic membrane*, inside of which the pyogenic bacteria have finally perished from starvation. These cold abscesses persist for months, even years, and may slowly disappear by well-known changes, while the patient presents few, perhaps no signs of fever, sepsis, nor of any trouble. In other words, so long as bacteria can live and migrate, the fluid in which they disport themselves is pus, true pus; the fluid of an old cold abscess is, according to this view, no longer pus. It was pus once; it is now *puruloid* in a second sense.

I have tried often to make cultures of pyogenic bacteria from this material and failed, for reasons just stated; so have many other observers failed, and our position in this matter is indisputably the correct one.

Garré has made a careful study of a number of cold abscesses, and with the exception of a few arising in lymph glands from which he could cultivate the staphylococcus pyogenes aureus, the only bacterial elements he could find were tubercle bacilli. These were with difficulty recognized by culture tests, but always by the result of inoculation. He contends that the view that pyogenic cocci had been present, but had been destroyed, can scarcely be entertained, since the pus out of these very abscesses could be used as a culture medium for the same pyogenic cocci, which could not be the case had their kind perished in it.

Garré concludes that so-called tuberculous pus is in reality not pus at all, but represents softened and separated necrotic caseous remains of previous tubercle elements. It contains mainly cell fragments and albuminated or fatty detritus, in con tradistinction to the pus of acute abscesses which contains well formed pus cells.

The relative infrequency of tubercle bacilli in such pus, and the difficulty of recognizing them even by cultivation, or in any way save by inoculation, leads him to the hypothesis that this material owes its infectiousness rather to the presence of tubercle *spores* than to the adult bacilli, the former finding only in living tissues the condition requisite for their growth.

Garré's views as to the nature of tubercular puruloid are corroborated by Baumgarten, as well as by Terillon. (Prog. Med., 1887, No. 2.) (Deutsche Med. Woch., 1886, 34, p. 581.)

Tricomi, after investigations concerning the ordinary periarticular abscesses of tubercular joint disease, claims that so long as they remain closed they never contain pyogenic cocci, but only tubercle bacilli, if any. (Giorn. Internaz. dell Scienze Mediche, 1886, 6, p. 628.)

The conspicuous difference between the teaching of 1871 and that of to-day obtains in this, that the degree of inflammatory disturbance necessary for the production of pus is not produced by mechanical nor thermal lesions alone, nor by even chemical irritants, except under most peculiar conditions. All suppurations met with in practice are due to bacterial agency, but mainly when, through this agency, nourished within the tissues or planted upon absorbent wound surfaces, they propagate themselves and give forth their peculiar chemical products, *i. e.*, ptomaines. Still, even then, without some predisposing lesion or condition in animals and men, in tissues capable of resorption, the commonly known pyogenic cocci are innocuous.

To this fortunate fact it is due that not every wound suppurates which is not immediately provided with an antiseptic dressing.

While there is, virtually, no pus without bacteria, the reverse is not necessarily true; for we may have even pyogenic cocci present in relatively very small numbers without formation of pus. A careful study of these cases shows them to be those in which suppuration is imminent but not yet absolutely existant. For instance, there may be present a mild degree of swelling, with an albuminous exudate, all of which may be resorbed without pus formation. Whether we are to look with favor, or not, upon Metschnikoff's explanation of the disappearance of the relatively few bacteria present in such cases, is a matter which I hesitate to discuss, though, for my own part, I certainly think it offers a most attractive and reasonable explanation. Virchow's vivid picture of the "battle of the cells" surely loses nothing from Metschnikoff's treatment of the same subject, and phagocytosis is not yet disproved.

Virchow introduced the term "metastatic," and taught us what metastatic abscesses are, and the embolic process by which they are formed. This term also loses nothing of its significance in the light of recent enlargements of our knowl-

edge. The emboli which cause them are themselves infected, or even individual germs may be transported *via* the blood current as most minute emboli, and the only uncertain or unappreciated feature of this part of the subject is the determination of why minute and metastatic abscesses appear in one place and not in another. This may be, in some cases, the result of pure accident. In general, it compels us to fall back upon the explanation of a *locus minoris resistentiæ*. This may be some mechanical lesion, perhaps one too minute for our vision, or some fracture or previous inflammatory focus. Points of least resistance certainly do exist, though what constitutes them such may be beyond our ken. No one can long study minute pathology without being convinced that there may occur a certain vulnerability of tissue, so to speak, for which we can offer no suitable explanation. The communication of contagion from one person to another is common evidence of this fact. Tissues, then, which suppurate are vulnerable in this respect: they succumb from not having the power to resist infection—that is, the invasion of their bacterial enemies, and the pus is the evidence of the conquest of vegetable cells over animal cells.

The matter is a difficult one to treat of. We have forms and forms of pus-formation. As Grawitz has shown, we have to deal with pus under at least four apparently different circumstances:

1. Cases of typical pyæmia.
2. Abscesses at points of least resistance.
3. Apparently spontaneous suppurations; *e. g.*, acute osteomyelitis.
4. Abscesses at points where there has been previously an inflammation.

He and Rinne have pointed out that the localization of pyogenic cocci is an affair of local determination, of interference with absorption, of chemical poisoning (through the circulation), of local ischæmia, etc.; in other words that by existing local irritations, by beginning inflammatory disturbances, or by regenerative cell-proliferations, in spite of previously held opinions, the metastatic grouping of cocci is absolutely prevented.

Rinne divides suppurations into two groups:

1. Those determined by bacteria of peculiar activity, whose attack upon the organism is vigorous; *e. g.*, tuberculosis, actinomycosis, epidemic cerebro-spinal meningitis, are caused by such organisms as seem to have a peculiar virulence, aside from any pyogenic properties.

2. Those determined by the members of the now well-known group of pyogenic cocci, particularly including staphylococci and streptococci.

We are confronted in this study by a most significant fact, which is very difficult of explanation. We have experimental proof that pyogenic cocci may be introduced into the tissues in no inconsiderable number—the same thing occurring every day in many accidental ways—that they may even be found circulating in the blood, without calling forth either suppuration or notable inflammation. According to the researches of Wyssokowitsch they do not escape by the kidneys. What, then, does become of them? It would appear, Grawitz says, that (*a*) they are dissolved, and disappear in the blood and other fluids; or that (*b*) there is an active conflict between them and the cells, a struggle for existence, which Virchow, as stated, has already called "the battle of the cells." The best known defender of the first view is Baumgarten, while Metschnikoff's name is most prominently associated with the second. Here again, there is really much to be said on each side, and there seems to be no reason why each may not be right. According to Grawitz the cocci usually die in pus after six to ten days, that is at a time when cell activity in the pus has ceased. Beyond a certain point increase of cocci is impossible in pus since the fluid becomes a too concentrated albuminoid material for them, just as syrups are too strong sugary solutions for the growth of fermentative and other organisms. On blood-clot they do not grow, though they will on blood-serum. Active penetration of cocci into white corpuscles is out of the question; therefore, when they are found in the interior of leucocytes, the latter must be regarded as the active agents. Certainly cocci are found inside the pus-cells, for anyone may see them there, and pus-cells, if we know anything about pus, were many of them originally leucocytes.

Certainly, too, one cannot say which he has to deal with, when isolated, a pus-cell or a leucocyte, unless he finds it containing one or more cocci imbedded in it.

If, then, in this battle of the cells, when once infection has taken place, the parasites are victorious, whether from overwhelming numbers, or from finding their enemies weakened from disease, then the infection of the surrounding tissues extends, and metastatic abscesses may finally or speedily result in the patient's death. On the other hand, if the tissue elements can successfully resist, then the battlefield is surrounded by a wall of young cell elements, which are very rapidly proliferated, and we have only a local abscess, in whose walls certainly takes place some of the phagocytosis which Metschnikoff has so successfully described. The course of that particular suppurative process is henceforth determined, not so much by production of some ptomaine, as by the reaction of the cell elements most concerned. So soon as the bacteria die or are killed, in case the pus has not been evacuated, the pus-cells undergo fatty metamorphosis, gradually disappear by absorption, or perhaps caseate in part; for an indefinite time there remains a concealed scar to mark the site of the old battleground, and finally all local and general damage is repaired.

The minute mechanism of abscess formation is of no small interest. Where infection occurs through the blood, the organisms are deposited in the smaller capillaries in the form of minute emboli, as is seen in pyæmia, and their first effect is the change in the tissues so well described by Weigert under the name of coagulation-necrosis. Sections through the periphery of such abscesses show that in immediate proximity to the central purulent mass there is a zone of tissue which takes no stain, and which presents a homogeneous translucent appearance, evidently resulting from the action of concentrated products of the micro-organisms, or from their own action, and constituting the coagulation-necrosis. If examined at the proper time a second zone appears outside this, which is composed of a dense mass of leucocytes, apparently collecting where chemical substances are more dilute and interfere less with cell life. The first zone becomes infiltrated on the one

hand with cocci from the infected center, and on the other hand with cells from the outer rim, and, with the original tissue, rapidly disappears, probably largely owing to the result of the peptonizing action of the cocci. Meanwhile, for the same reason doubtless, the effused fluid does not coagulate, and thus we have a central collection of fluid containing leucocytes and cocci, that is, an abscess. When cocci spread into tissue after injection, or from infection of the skin, they usually at first follow the course of the lymph canals, and we find a central area of yellowish appearance containing leucocytes and cocci, surrounded by an inflamed area infiltrated with the same. The cocci, according to the density of the tissue spread in masses or singly, forming, in loose tissue, small groups or chains of a few individuals, the cellular elements swelling up and forming a homogeneous mass (coagulation-necrosis) ultimately undergoing liquefaction as before. Outside of this a zone of leucocytes is formed for the purpose of withstanding the onset and checking the progress of the micro-organisms. After a few days they usually get the upper hand, and the acute process is at an end. In the case of proteus vulgaris, which causes abscesses in rabbits, and of the bacillus of chicken cholera, which causes abscesses in guinea pigs, there is a mass of necrotic tissue in the interior of the abscess which is left undissolved on account of their feeble peptonizing power. The only difference, practically, between abscess and purulent infiltration is the circumscribed or indefinite boundary of the area involved. The principal difference between abscess and carbuncle is that in the latter there is no such perfect solution of dead tissues and cells. The coagulation-necrosis appears to involve such a mass of tissue at once that its solution and escape as pus is impossible. The bacillus of chicken cholera causes abscess in the guinea pig, and the proteus vulgaris causes them in rabbits, and in each case there is left a mass of necrotic tissue in the interior of the abscess whose solution has failed, perhaps on account of the feeble peptonizing power possessed by these organisms.

In man the chain of events is nearly the same as in the lower animals, save that they occur perhaps more quickly. The description above given refers more especially to abscess caused

by staphylococci. The streptococci seem to have a slightly different method of action, and it may be that the differences between the two species are due, in some respect, to their varying peptonizing power.

Herein, too, we see the difference between recent and old abscesses, in respect to the so-called "pyogenic" membrane. The protective cell elements thrown out about an infected spot, as alluded to above, are a matter of hours, or, at most, of a few days' existence. No time is afforded for organization, nor is it desired. They are meant to serve only as a temporary barrier. Consequently, in an acute abscess we must not expect to find any such membrane, and, if it is folly to look for it, how much more so to describe it, as some have attempted to do. Only in the subacute abscess, or for some weeks pent-up collection of pus, can we find anything approaching it. But it is in the cold abscess, the long-existing one, *par excellence*, that we find a membrane or lining which can be peeled or stripped off; though it is a sad misnomer to call it a pyogenic membrane, since it is anything but this. It is the result of the organization and condensation of this zone of protective cell elements, which were thrown out when the infection and the encroachment were new, which was supposedly intended to be temporary, but has persisted as long as that encroachment from which it was originally intended to protect, and which has grown old and hardened in this service. It is no more pyogenic in the strict sense of the term than it is chromogenic, and its name should be dropped for a better term. If we must have a descriptive name for this membrane, and it is well that we should, I would like to suggest that we call it *pyophylactic*, as indicating clearly its function if not its appearance.

Pus proper comes to our notice in four ways:

1. In circumscribed subcutaneous collections of new formations—acute abscess.

2. From the surfaces of shut sacs and cavities—empyæmas.

3. On exposed tissue surfaces and granulating wounds—pyorrheas.

4. In the shape of purulent infiltration of subcutaneous tissues, more or less deeply occurring.

Pus proper, then, is a mixture of originally good cellular

materials infected and gone to the bad, suspended in fluid more or less albuminous, and containing at times adventitious substances, like biliary or hæmic coloring matter, tissue shreds, etc.

When pus-cells have undergone fatty changes, when vital activity of all cells, parasitic or otherwise, has subsided, and when more or less of the fluid portion has been absorbed, leaving more concentrated, semi-fluid or solid residue—and when this has perhaps undergone caseous degeneration, then this material is not pus in the sense in which I am using the term, whatever it may have been originally. So long as it has the general appearance of pus, I would suggest for it the name *pyoid* or *puruloid*. When it is caseated, or is so thick that it does not flow, I would suggest that we then call it *archepyon*, that is to say, "originally pus."

I introduce these new names to you with considerable hesitation and with becoming modesty, yet I am convinced that if we had names for the different materials, or the different conditions of the same material, it would conduce to clearer notions concerning the substances themselves.

Certain conclusions based upon the above study may be formulated here, as follows:

1. Inflammation is, in effect, a disturbance of cell nutrition, along with cell proliferation, causing a recurrence to the embryological condition of certain of the cells of the tissue most involved.

2. This embryonal condition means a reversion to the form of those medullary or indifferent corpuscles, from which in the beginning of its normal development the tissue was built up.

3. Congestion, and even stasis, though they precede inflammation, do not necessarily cause it. They may subside before cell nutrition has had time to suffer. They may simply cause temporary cell activity.

4. Medullary, indifferent, or embryonic cells arise not only from the recognized cells of the tissue, *i. e.*, its active protoplasmic elements; it is probable that the intercellular or basis substance, which was originally produced from embryonic tissue, may again give rise to them.

5. When such new formed embryonic cells advance again

to the condition of basis substance, much of the inflammatory new formation has subsided. When with this is coupled restoration to the circulation of exuded fluids and such red and white blood corpuscles as are capable of return, and when all other newly formed cells are liquefied and absorbed, then the process of *resolution* is complete.

6. When both inflammatory and new embryonic cells establish a reticular intra-connection, then we have a true hyperplasia.

7. When into this collection of cells, parasitic vegetable cells (bacteria) are intruded, no matter how, blood-vessels break asunder, basis substance is dissolved, the individual animal cells are attacked, and these are now suspended in an albuminous fluid and represent pus corpuscles, and we have a collection of pus.

8. Pus-cells are no longer fit for any useful purpose, but constitute a source of offence. Henceforth they are treated as foreign bodies, of which the tissues endeavor to rid themselves at once. Nature extrudes them in the direction of least resistance, and hence we have the well-known phenomenon of the "pointing" of the abscess.

9. So far as we can learn, bacteria, and bacteria alone, can determine, in the human body, such a series of changes as lead to the formation of pus, *i. e.*, pus within the meaning to which I have endeavored to confine it. Whatever results may follow experimental introductions of a few chemicals into the tissues of some of the lower animals, such experiments find no parallel in our clinical experiences. Moreover, as stated above, the product of such experiments is not pus, but puruloid; it lacks the essential pathogenic and noxious elements of pus,—the micro-organisms which confer upon it its infective and toxic properties.

10. We are then prepared to make the brief and explicit statement that, *clinically* at least, we have no suppuration except such as is produced by bacteria; in other words, that pus is a product of parasitic origin.